REMARKS

The specification has been amended to reflect the 371 status. The original figures have been replaced with the substitute figures submitted during prosecution of the international application.

Lastly, claim 46 has been clarified, which amendment is clear from the wording of claims 47 and 48.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned "**Version with markings to show changes made**".

Favorable action on the merits is solicited.

Respectfully submitted,

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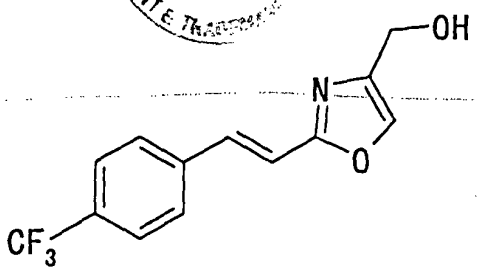
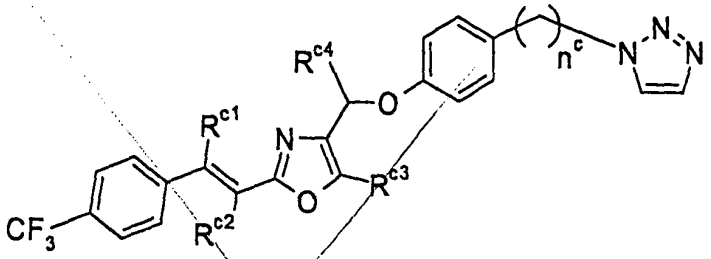
December 28, 2001

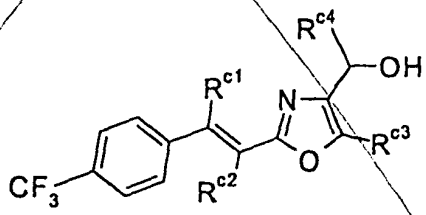
Version with Markings to Show Changes Made



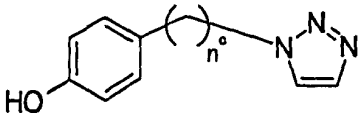
45. A method for producing a compound of the formula



wherein n^c is an integer of 1 to 10 and other symbols are as defined in claims 32, or a salt thereof, which comprises subjecting a compound of the formula



wherein each symbol is as defined above, or a salt thereof to sulfonylation or halogenation, and reacting the resulting compound with a compound of the formula



wherein n^c is as defined above, or a salt thereof.

(Amended), A crystal of

46. 1-[4-[4-[[2-[(E)-2-[4-(Trifluoromethyl)phenyl]ethenyl]-1,3-oxazol-4-yl]methoxy]phenyl]butyl]-1H-1,2,3-triazole.

47. The crystal of claim 46, having characteristic peaks at diffraction angles of 6.98, 14.02, 17.56, 21.10 and 24.70

SPECIFICATION

PRODUCTION METHOD OF 1-SUBSTITUTED-1,2,3-TRIAZOLE DERIVATIVES

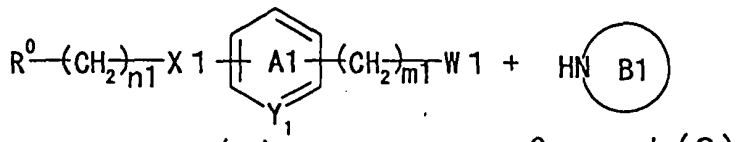
this application is a 371 of PCT/JP01/06145 filed July 16, 2001

TECHNICAL FIELD

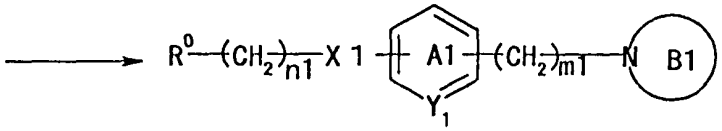
The present invention relates to production methods of intermediates for 1-substituted-1,2,3-triazole compounds having an inhibitory action on growth factor receptor tyrosine kinases (especially HER2) useful as pharmaceutical agents.

BACKGROUND ART

As a production method of an intermediate for a 1-substituted-1,2,3-triazole compound having a tyrosine kinase inhibitory action, for example, there is mentioned a method comprising condensing compound (1) of the following formula and compound (2) of the following formula in the presence of a base in a solvent inert to the reaction (e.g., aromatic hydrocarbons such as benzene, toluene, xylene etc., ethers such as tetrahydrofuran, dioxane etc., ketones such as acetone, 2-butanone etc., halogenated hydrocarbons such as chloroform, dichloromethane etc., N,N-dimethylformamide, dimethyl sulfoxide, and a mixed solvent of these) to give the objective compound (3) (JP-A-11-60571, WO 98/03505):



Compound (1) Compound (2)



Compound (3)

wherein W1 is a leaving group, R^0 is an optionally substituted aromatic heterocyclic group, X1 is an oxygen atom, an optionally oxidized sulfur atom, -C(=O)- or -CH(OH)-, Y_1 is CH or N, m1 is an integer of 0 to 10, n1 is an integer of 1 to 5, the cyclic group